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Case Report

Locally advanced invasive lobular carcinoma presenting as skin erythema, with multimodality imaging correlation ☆,☆☆

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ABSTRACT

Invasive lobular carcinoma comprises 10-15% of invasive carcinomas of the breast. Its inconspicuous pattern of proliferation may lead to tumor manifestations that can be challenging to detect on mammography and clinical exam, which can result in tumor detection at advanced size and stage. This case demonstrates a locally advanced invasive lobular carcinoma and its subtle growth pattern illustrated on several imaging modalities, as well as its unique initial clinical presentation of skin erythema mistaken for rash.

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Introduction

Aside from skin cancer, breast cancer is the most commonly diagnosed malignancy for women in the United States, expected in 1 of 8 women over the course of their lifetime [1]. The 2 most frequently encountered histologic subtypes of breast cancer are invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC), with the latter comprising 10-15% of invasive carcinoma cases [2–4]. Despite its lower incidence, the unique growth pattern of ILC can provide challenges for radiologists and pathologists in detecting this tumor as well as

for surgeons when excising it. This case highlights the subtle growth pattern of a primary invasive lobular carcinoma, demonstrated on several imaging modalities, as well as its noteworthy clinical presentation.

Case report

A 79-year-old woman presented with a 2-week history of an erythematous nonpruritic rash involving the skin of the superior left breast. The patient denied trauma, new clothing/detergents, or skin allergies, and was prescribed hydrocortisone cream for twice daily application. Over the next 6

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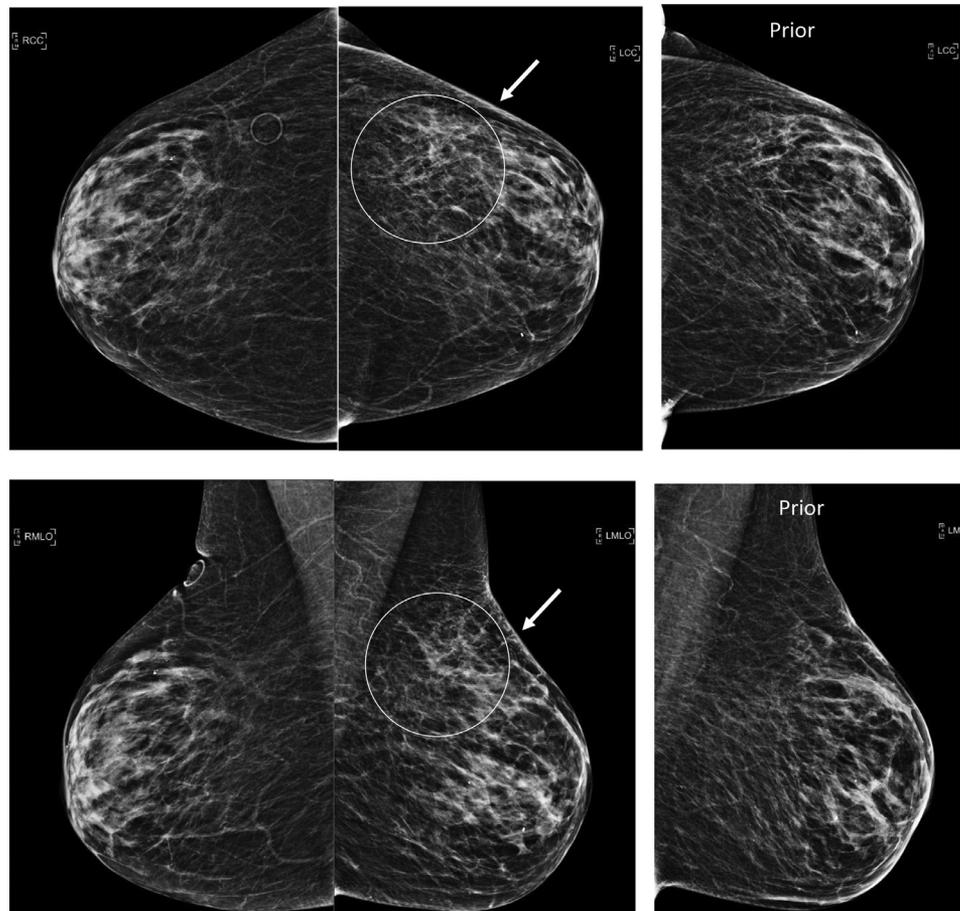


Fig. 1 – Current bilateral screening mammogram (left images) showing skin thickening (arrow) and trabecular thickening (circle) in the upper-outer left breast, representing an interval change from the prior mammogram (right images).

months, there was an interval decrease in size of the rash, but focal residual skin redness persisted in a small isolated portion of the upper-outer quadrant.

Screening mammogram demonstrated focal skin and trabecular thickening in the upper-outer left breast, therefore additional imaging and clinical exam were recommended (Fig. 1). Diagnostic mammogram showed persistent skin and trabecular thickening, and a targeted ultrasound revealed subjacent heterogeneous tissue echotexture without discrete mass (Fig. 2). Dedicated clinical exam confirmed palpable focal erythematous skin changes in the upper-outer left breast. A skin punch biopsy was recommended and yielded invasive lobular carcinoma, Nottingham grade 1 (estrogen receptor positive, progesterone receptor positive, and HER2 equivocal), involving the dermis and subcutaneous tissue (Fig. 3). Staging breast MRI and PET/CT exams were performed (Fig. 2). MRI showed skin thickening with associated dermal enhancement in the upper-outer left breast as well as a subjacent infiltrative mass plus nonmass enhancement spanning 6 cm, correlating with the trabecular thickening seen on mammogram. ^{18}F -FDG PET/CT demonstrated left upper-outer breast skin thickening with associated minimally increased uptake (standardized uptake value, SUV, of 1.5).

The patient was treated with neoadjuvant endocrine therapy (letrozole) and palbociclib for 5 months with subsequent

breast MRI and PET/CT demonstrating complete imaging response of the prior abnormalities in the left breast. A left breast modified radical mastectomy was performed with negative margins, and a left axillary dissection showed 26 lymph nodes negative for carcinoma. The patient has had no evidence of recurrent malignancy at 3 years of follow-up.

Discussion

Invasive lobular carcinoma can offer considerable challenges in detection due to its pattern of proliferation. The targeted disruption of E-cadherin is inherent to ILC, which results in a dysregulation of cell adhesion and a characteristic discohesive growth pattern [4,5]. The tumor often grows via stromal invasion by single cells or single files of cells, resulting in minimal disruption of the normal tissue architecture [1]. Anatomic structures are preserved during early tumor growth and the associated desmoplastic reaction, if present at all, is often far less prominent than that seen with invasive ductal carcinomas [6]. Therefore, ILC often fails to form a palpable mass and is challenging to detect on clinical exam [7]. These growth characteristics result in lower mammographic and sonographic sensitivities for detection of ILC compared

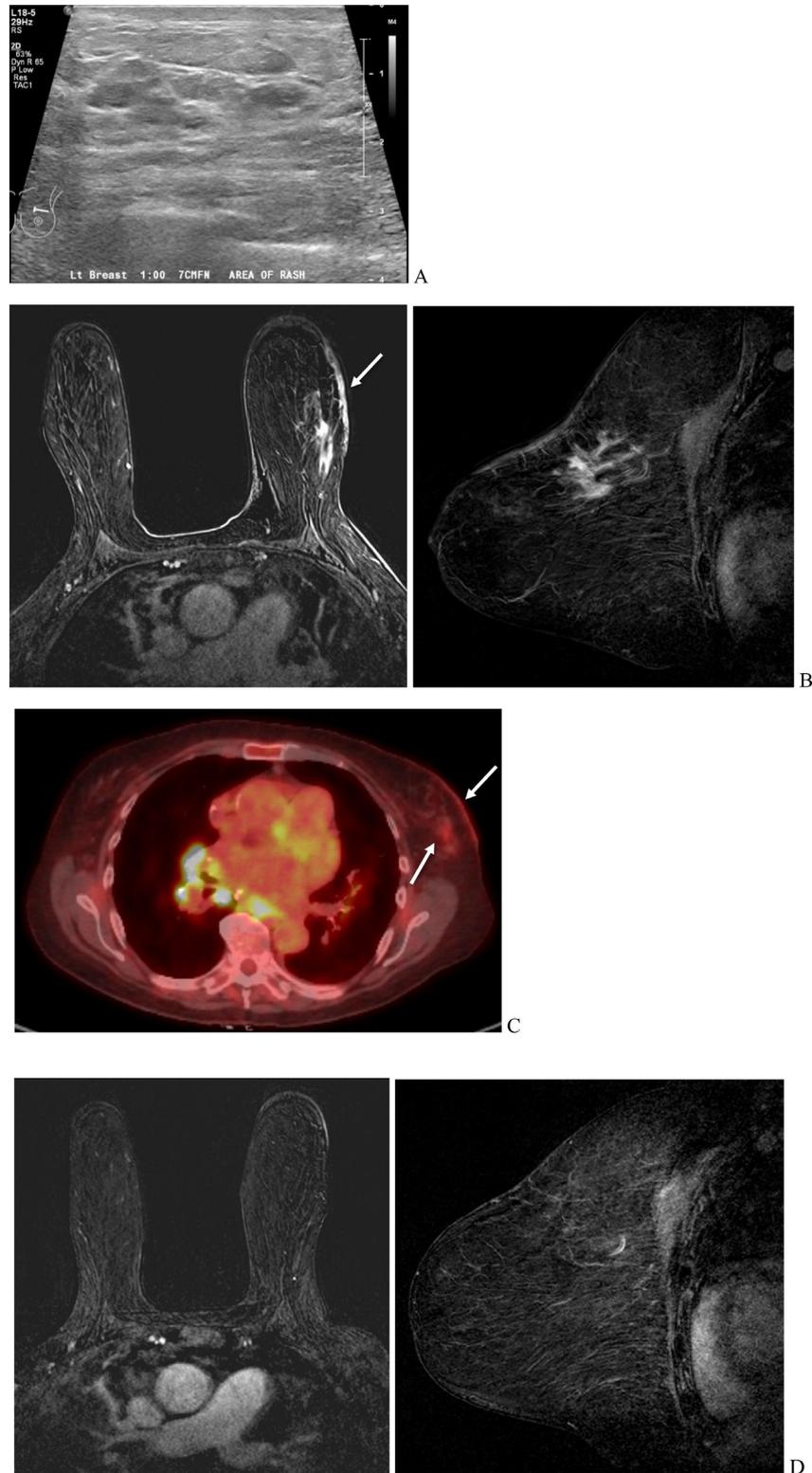


Fig. 2(A) – (A) Grayscale ultrasound image showing nonspecific hypoechoic tissue subjacent to the skin erythema, but no discrete mass. (B) Axial (left image) and sagittal (right image) subtraction images from contrast-enhanced MRI showing mass/nonmass enhancement in the upper-outer left breast, with associated skin enhancement and thickening (arrow). (C) ^{18}F -FDG PET/CT showing mild FDG uptake associated with the left breast mass and skin (arrows). FDG-avid mediastinal adenopathy attributable to sarcoidosis, with long-term imaging stability. (D) Axial (left image) and sagittal (right image) subtraction images from post-neoadjuvant treatment MRI showing resolution of prior abnormal enhancement in the left breast.

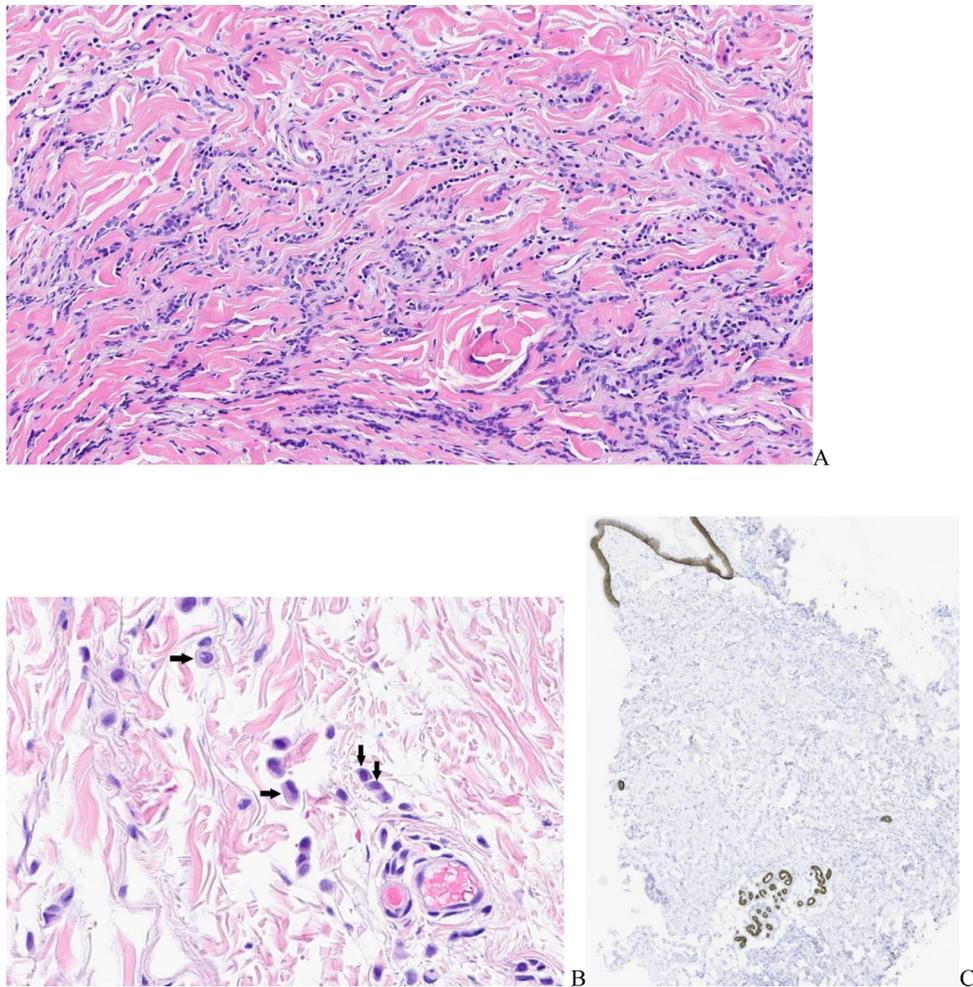


Fig. 3(A) – (A) Histologic section of skin punch biopsy at intermediate power demonstrating diffuse infiltration by a dyshesive, low-grade malignancy arranged in single file pattern with minimal desmoplasia (hematoxylin & eosin stain, 13x magnification). (B) High power view illustrating cellular dyscohesion and single cell infiltration of tumor cells, with most cells showing minimal cytomorphic atypia with mildly enlarged nuclei and some prominent nucleoli (arrows) (H&E stain, 40x). (C) E-cadherin immunohistochemical stain showing negative staining within the tumor cells, supportive of lobular type, while the internal controls (skin and adnexal structures) react appropriately (E-cadherin immunohistochemical stain, 1x).

to IDC, as well as potential underestimation of ILC size which may hamper the surgeon's ability to obtain negative margins [6,8,9]. ILC tumor extent is best delineated on breast MRI [10]. Invasive lobular carcinomas tends to be larger and at later stages at the time of diagnosis, with higher rates of multifocality and bilaterality, and have unique metastatic spread patterns including gastrointestinal/genitourinary tracts, serosal surfaces, and the leptomeninges in addition to the more classic osseous, lung, and liver metastases [4,6,11,12].

Mammographic presentation of ILC is most commonly a mass, followed by architectural distortion and asymmetries. Masses can be of equal- to low-density and may be less conspicuous than denser IDC masses [1,2]. False-negative rates for mammographic detection of ILC are estimated at 19-43%, with 35% of lesions visible on a single view [3,9,13]. Sensitivity for ILC in dense breasts is even lower, with some estimates at 8-11% [4,14]. Sonographic appearance of ILC can vary from hy-

poechoic masses to ill-defined areas of inhomogeneous echotexture or nonspecific shadowing, with estimated sensitivity for detection of 68-98% [4,15]. MRI has the highest sensitivity for detection at 93-96%, providing exquisite detail of mass and/or nonmass extent, and has shown value in preoperative surgical planning [1]. On the other hand, primary ILC on ^{18}F -FDG PET is often more challenging to detect with a characteristically lower SUV compared to IDC [16].

This case demonstrates classic imaging features of primary ILC on multiple imaging modalities. The inconspicuous growth pattern in this case resulted in progression of a superficial tumor to locally advanced disease with invasion of the adjacent dermis. Skin invasion was the first clinically evident manifestation of disease, but skin erythema was temporarily misidentified as a rash. When associated mammographic changes were noted, suspicion level increased, and punch biopsy led to the diagnosis. ILC presenting as a skin

lesion is uncommon with sparse case reports. However, cases show that dermal lesions can represent malignant processes and should be treated with higher clinical suspicion when associated with palpability, as seen here [17]. This case also serves as a reminder that persistent clinical abnormalities may require tissue diagnosis in the absence of imaging findings, which might have led to the diagnosis sooner than its ultimate detection on subsequent mammogram. While diagnosis of ILC remains challenging on mammography, digital breast tomosynthesis can increase lesion conspicuity [6]. Supplemental screening exams with functional imaging approaches also show promise in improving detection, especially in women with dense breasts.

Conclusion

Due to their inconspicuous growth patterns, invasive lobular carcinomas present challenges in mammographic detection and delineation of extent, often presenting at larger sizes and later stages than invasive ductal carcinomas. Mammographic interpretations require careful attention for interval changes, as manifestations are often subtle and less likely to present with palpable masses on clinical exam.

Patient consent

Written informed consent was obtained from the patient for publication of this case report.

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